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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/980,516	04/03/2002	Michel G. Bergeron	GGD-31611-PCTUS	5405

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EXAMINER	
HUYNH, PHUONG N	
ART UNIT	**PAPER NUMBER**
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/980,516	BERGERON ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-10,12-20 and 24-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-10,12-20 and 24-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 April 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/29/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/20/06 has been entered.

2. Claims 4-10, 12-20 and 24-27 are pending and are being acted upon in this Office Action.

3. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: The specification fails to provide antecedent basis for the term "liposome comprises a mixture of diacylphosphatidylcholine:diacylphosphatidylglycerol:diacylphosphatidylethanol-amine-polyethyleneglycol in a molar ratio of **10:3:0.1-3**." in *original* claim 7.

Likewise, the specification fails to provide antecedent basis for the term "distearoylphosphatidylcholine:distearoylphosphatidylglycerol in a molar ratio of 10:3" in *original* claim 8 lines 3-4 and

"liposome comprises dipalmitoylphosphatidylcholine:dipalmitoylphosphatidylglycerol: dipalmitoyphosohatidylethanolamine-polyethyleneglycol in a molar ratio of 10:3:0.33" in *original* claim 9.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 4-10, 12-20 and 24-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.**

The recitation of "***about*** 10:1 to 1:1" in amended claims 24 and 26 represents a departure from the specification and the claims as originally filed. The passages pointed out by applicant in the amendment filed 11/20/06 do not provide a clear support for the said phrase. In fact, the specification at page 6, line 36-37 and original claim 3 disclose a mixture of diacylphosphatidylcholine and diacylphosphatidylglycerol in a molar ratio ranging ***between*** 10:1 and 1:1. The term "about" broadens out the molar ratio *between* 10:1 and 1:1. Claims 4-5, 7-10, 12-20 and 27 are included in this rejection because said claims depend from rejected claim 24.

The recitation of "the formulation which comprises an anti-HLA-DR antibody molecule coupled to a liposome, said antibody molecule being selected from the group consisting of a whole antibody and an antibody antigen binding fragment thereof, said formulation capable of binding to an HLA-DR protein present at both the surface of an infectious agent and at the membrane surface of a cell, wherein said liposome comprises a mixture of diacylphosohatidylcholine and diacylphosphatidylglycerol wherein the molar ratio is **10:3**" in claim 6 represents a departure from the specification and the claims as originally filed. This is because the specification does not disclose the formulation wherein the liposome comprises diacylphosohatidylcholine and diacylphosphatidylglycerol wherein the molar ratio is **10:3**. The specification at page 7, lines 6-7 discloses the formulation wherein the liposome comprises dipalmitoylphosphatidylcholine (DPPC):dipalmitoylphosphatidylglycerol (DPPG) in a molar ratio of 10:3.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

7. Claim 6 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 recites the limitation "molar ratio is 10:**3**". There is insufficient antecedent basis for this limitation in the claim. This is because base claim 24 recites "molar ratio of 10:**1** to 1:**1**".

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 4-8, 12-16, 19-20 and 24-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No. 5,773,027 (of record, issued June 30, 1998; PTO 892) in view of Catin et al (of record, J Virology 71(3): 1922-1930, March 1997; PTO 892).

The '027 patent teaches various formulations for treatment of viral disease such as HIV which comprise an antibody coupled to various liposomes such as liposome that comprises a mixture of diacylphosphatidylcholine and diacylphosphatidylglycerol in a molar ratio ranging between 10:1 and 1:1, wherein the acyl chains are either saturated or unsaturated and have between 14 and 18 carbon atoms in length (palimitoyl is 16 carbons while stearoyl is 18 carbons in length) (See claim 1 of '027 patent, col. 3, lines 58-62, in particular). The '027 patent further teaches liposome comprising a polyethyleneglycol derivative of diacylphosphatidylethanolamine (see claim 2 of '027 patent, in particular). The reference formulation wherein the liposome comprises a polyethyleneglycol derivative of diacylphosphatidylethanolamine and wherein the polyethyleneglycol has a molecular weight between about 500 and 5000 Daltons (See claim 11 of '027 patent, in particular). The '027 patent also teaches a formulation wherein the liposome comprises a mixture of diacylphosphatidylcholine (DPPC) and diacylphosphatidylglycerol (DSPG) in a molar ratio of 10:3 (See col. 3, lines 46-47, in particular). The '027 patent teaches another formulation wherein the liposome (lipid component) comprises a mixture of diacylphosphatidylcholine (DPC): diacylphosphatidylglycerol (DPG): diacylphosphatidylethanol-amine-polyethyleneglycol (DPE-PEG) in a molar ratio of 10:3:1.45 (See col. 5, lines 48, col. 9, Table 3, line 39, in particular). The reference molar ratio of 10: 3:1.45 is within the claim range

of 10:3:0.1-3. The reference formulation further encapsulated a drug such as AZT, ddI, ddC, saquinavir, ganciclovir, foscarnet and ribavirin for treating viral infection (See claims 7, 9-10 of '027 patent, in particular). The '027 patent further teaches that the reference liposome formulation can be modified by coupling of antibody molecules to enhance the targeting of the liposome to the specific cells (See col. 4, lines 11-13, in particular) that are HIV reservoirs as well as marked improvement of the pharmacokinetics of drugs (See abstract, in particular). The advantages of targeted delivery of anti-viral agents encapsulated in liposome are that it could increase efficacy by reducing toxicity of anti-viral agents in humans suffering from AIDS or other viral diseases, improving drug bioavailability upon encapsulation of drugs into liposome that could reduce the dose of anti-viral agents used in conventional therapy as well as reducing the frequency of administration of anti-HIV agents and therefore improving the quality of life of patients with AIDS and other viral diseases as taught by the '027 patent (See col. 2, lines 25-31, col. 9, lines 7-12, in particular). The drug-liposome formation also increases the drug uptake by macrophages such as RAW 264.7 (see col. 7, lines 4-8, in particular).

The claimed invention differs from the teachings of the reference only in that the formulation which comprises an anti-HLA-DR antibody instead of any antibody coupled to the liposome wherein the formulation capable of binding to an HLA-DR protein present at both the surface of an infectious agent and at the membrane surface of a cell.

Catin et al teach antibody such as anti-HLA-DR 2.06 (class II MHC) that binds to HLA protein present at the surface of an infectious agent such as HIV-1 virions and at the surface of a host cell membrane such as CD4+ T cells and macrophage (see entire document, page 1923, col. 2, Antibodies, page 1925, col. 1, page, in particular). Catin et al teach infectious agent such as HIV acquired host protein such as HLA-DR, ICAM-1 (CD54), CD55 (DAF), CD59, CD63 and CD71 (see page 1922, col. 1, in particular). Catin et al teach antibody to HLA-DR or anti-LFA-1 (CD11a) inhibits HIV infection since HIV virus acquired host cellular protein on the surface of the progeny virus (see page 1922, col. 1, in particular). Catin et al further teach CD4 molecule is the primary cell surface receptor for HIV-1 (page 1922, col. 2, in particular). Catin et al teach HLA-DR protein is one of the most abundant host derived protein acquired by virus such as HIV-1 and HIV-2 (see page 1922, col. 2, in particular). The reference HLA-DR protein is expressed in lymphoid cells such as CD4+ T lymphocytes, and monocyte derived macrophages or antigen presenting cells within the reticuloendothelial system (lymph node) (see page 1922, col. 2, in particular). Catin et al teach HIV-1 infectivity is enhanced by the presence of virally

incorporated host cell membrane (see page 1925, col. 2, last paragraph, page 1927, col. 2, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the antibody coupled to a liposome that comprises a mixture of diacylphosphatidylcholine and diacylphosphatidylglycerol in the formulation as taught by the '027 patent for the specific anti-HLA-DR antibody that binds to HLA-DR on the surface of infectious agent and host cells as taught by the Catin et al. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because the '027 patent teaches coupling of antibody molecule to a liposome enhances the targeting of the drug encapsulated in the liposome to the specific cells that are HIV reservoirs as well improving the pharmacokinetics of drugs (See col. 4, lines 11-13, abstract, in particular). Catin et al teach HLA-DR protein is one of the most abundant host derived protein acquired by HIV-1 and HIV-2 and HLA-DR protein is expressed on the surface of host lymphoid cells such as CD4+ T lymphocytes, and monocyte derived macrophages which are an obvious target for such strategy (see page 1922, col. 2, in particular).

Applicants' arguments filed 11/20/06 have been fully considered but are not found persuasive.

Applicants' position is that claims 4, 6, 24 and 26 have been amended. EP0286418 does not teach the characteristic of the liposome as now amended. Saarloos et al discloses that HLA-DR (Class II MHC) was associated with in vivo sources of HIV-1 virions from primary isolates, macrophages and blood plasma using an immuneocapture method with an anti-HLA-DR antibody, the results showed that the anti-HLA-DR antibody capture about 50% of HIVAda-M and HIVBa-L monocytotropic virus, and four of eight samples of plasma virus did not detectably bind to the anti-HLA-DR antibody (see Saarloos at page 1641, 2nd col., 2, 2nd ¶). At most, Saarloos' disclosure presents an "obvious-to-try" situation. Given the unpredictability of the binding of an anti-HLA-DR antibody with HIV-1 virions and the level of HLA-DR expression in monocytes according to Saarloos, one skilled in the art reading Saarloo's disclosure would not expect an anti-HLA-DR antibody would necessarily and inevitably bind to HLA-DR protein on both a cell and on HIV virus – much less an antibody coupled to a liposome.

In response, the arguments with respect to the EP0286418 and Saarloos et al references are moot since the rejections using said references have been withdrawn and said references are no longer applied to this set of rejected claims. However, Catin et al, of record, teach HLA-DR antibody 2.06 (class II MHC) binds to HLA protein present at the surface of an infectious agent such as HIV-1 virions and at the surface of a host cell membrane such as CD4+ T cells and macrophage (see entire document, page 1923, col. 2, Antibodies, page 1925, col. 1, page, in particular). In fact, the same monoclonal antibody anti-HLA-DR (clone 2.06, IgG1) as taught by Catin et al was used by applicants, see instant specification at pages 12, line 7-8. One skilled in the art reading the specification would expect a monoclonal anti-HLA-DR 2.06 antibody from the same clone would necessarily and inevitably bind to the same HLA-DR protein on both host cell expressing HLA-DR and on HIV virions that have incorporated the host HLA-DR protein.

With respect to the argument that claims 24 and 26 have been amended to recite the specific liposome composition, the '027 patent, of record, teaches various liposome such as liposome that comprises a mixture of diacylphosphatidylcholine and diacylphosphatidylglycerol in a molar ratio ranging between 10:1 and 1:1, wherein the acyl chains are either saturated or unsaturated and have between 14 and 18 carbon atoms in length (palimitoyl is 16 carbons while stearoyl is 18 carbons in length) (See claim 1 of '027 patent, col. 3, lines 58-62, in particular). The '027 patent also teaches liposome formulation can be modified by coupling of antibody molecules to enhance the targeting of the liposome to the specific cells (See col. 4, lines 11-13, in particular). The advantages of targeted delivery of anti-viral agents encapsulated in liposome are that it could increase efficacy by reducing toxicity of anti-viral agents in humans suffering from AIDS or other viral diseases, improving drug bioavailability upon encapsulation of drugs into liposome that could reduce the dose of anti-viral agents used in conventional therapy as well as the frequency of administration of anti-HIV agents and therefore improving the quality of life of patients with AIDS and other viral diseases as taught by the '027 patent (See col. 2, lines 25-31, col. 9, lines 7-12, in particular).

11. Claims 10 and 17-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No. 5,773,027 (of record, issued June 30, 1998; PTO 892) in view of Catin et al (of record, J Virology 71(3): 1922-1930, March 1997; PTO 892) as applied to claims 4-8, 12-16, 19-20 and 24-27 mentioned above and further in view of Desormeaux et al (of record, J Drug Targeting 6(1): 1-15, 1998; PTO 1449).

The combined teachings of the '027 patent and Catin et al have been discussed supra. Catin et al further teach CD4 molecule is the major cellular receptor for HIV-1 for viral entry into host cell during the infection process and the CD4 is also a natural ligand of HLA-DR (see page 1927, col. 1, Discussion, in particular).

The invention in claim 10 differs from the combined teachings of the references only in that the formulation further comprising additional antibody that binds to CD4.

The invention in claim 17 differs from the combined teachings of the references only in that the formulation further comprising an additional antibody molecule that binds to one or more CD4 proteins.

The invention in claim 18 differs from the combined teachings of the references only in that the formulation further comprising an additional antibody molecule that binds to one or more CD4 proteins.

Desormeaux et al teach a formulation which comprises antibody and binding fragment thereof such as $F(ab)_2$ that bind specifically to CD4 molecules expressed on infectious agent such as HIV virus and CD4+ T cells and wherein the reference antibody or $F(ab)_2$ is coupled to a liposome for targeting liposome containing drug to CD4+ T cells, macrophages and viral particles (See entire document, abstract, page 3, col. 1, page 7, col. 1, last paragraph, in particular). The reference formulation further comprises an anti-viral drug such as AZT, ddC, foscanet, ddITP, (see page 3, col. 1, Drug containing liposome against HIV infection, in particular). Desormeaux et al further teach the advantage of using antibody binding fragment by removing the Fc fragment of an antibody instead of a whole antibody is that it reduces the immunogenicity of the antibody in immunoliposomes upon repeated administration (see page 6, col. 2, in particular). Desormeaux et al teach it is now well-established that CD4+ T cells and macrophages are the main reservoirs for HIV in infected individual and the advantage of using antibody directed liposome as a sustained drug carriers is that it target specific delivery of drugs encapsulated liposome to viral particles, macrophages and/or T cells in the lymphoid tissues (see page 11, col. 1, paragraph bridging pages 7 and 8, in particular). Desormeaux et al teach that site-specific drug targeting may allow less frequent administrations of anti-viral agents and at lower doses (therefore reduced toxicity) than convention therapy, and thereby improving efficacy, and quality of life for patients (see page 11, Advantages and Limitations, Table 1, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include additional antibody such as anti-CD4 or binding fragment thereof

that binds to one or more CD4 proteins acquired by the infectious HIV and CD4 expressed on the surface of host cells as taught by Desormeaux et al in the formulation comprising an anti-HLA-DR antibody molecule coupled to a liposome as taught by the '027 patent and Catin et al. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because Catin et al teach CD4 molecule is the major cellular receptor for HIV-1 for viral entry into host cell during the infection process and the CD4 is also a natural ligand of HLA-DR (see page 1927, col. 1, Discussion, in particular). Desormeaux et al teach it is now well-established that CD4+ T cells and macrophages are the main reservoirs for HIV in infected individual and formulation which comprises anti-CD4+ antibody or antibody binding fragment such as $F(ab)_2$ capable of targeting liposome encapsulated anti-viral drug to those viral reservoirs should lead to a reduction in the dissemination of HIV from the lymphoid tissue and to a preservation of the follicular dendritic cells microenvironment that would likely protect the infected host from developing the characteristic immunodeficient state (see paragraph bridging pages 7 and 8, in particular). Desormeaux et al teach that site-specific drug targeting may allow less frequent administrations of anti-viral agents and at lower doses (therefore reduced toxicity) than convention therapy, and thereby improving efficacy, and quality of life for patients (see page 11, Advantages and Limitations, Table 1, in particular). The '027 patent teaches coupling of antibody molecule to the liposome enhances the targeting of the drug encapsulated liposome to the specific cells that are HIV reservoirs as well as marked improvement of the pharmacokinetics of drugs (See col. 4, lines 11-13, abstract, in particular). Catin et al teach HLA-DR protein is one of the most abundant host derived protein acquired by HIV-1 and HIV-2; HLA-DR protein is expressed on the surface of host lymphoid cells such as CD4+ T lymphocytes, and monocyte derived macrophages which are an obvious target for such strategy (see page 1922, col. 2, in particular).

12. Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No. 5,773,027 (of record, issued June 30, 1998; PTO 892) in view of Catin et al (of record, J Virology 71(3): 1922-1930, March 1997; PTO 892) as applied to claims 4-8, 12-16, 19-20 and 24-27 mentioned above and further in view of Harlow *et al* (of record, in Antibodies a Laboratory Manual, 1988, Cold Spring harbor laboratory publication, Cold Spring Harbor, NY, pages 626-629) and Desormeaux et al (of record, J Drug Targeting 6(1): 1-15, 1998; PTO 1449).

The combined teachings of the '027 patent and Catin et al have been discussed supra.

The invention in claim 20 differs from the teachings of the references only in that the formulation which comprises an anti-Fab' antibody fragment against a HLA-DR instead of a whole antibody against HLA-DR.

Harlow *et al* teach a method of producing antibody fragment such as Fab fragment (See page 626-629, in particular). Harlow *et al* further teach that the problems of using multivalent antibodies on mammalian cells often will lead to capping and internalization of the antigen which can be overcome by using fragments of antibodies (See page 626 in particular).

Desormeaux et al teach the advantage of using antibody binding fragment by removing the Fc fragment of an antibody instead of the whole antibody when coupled to liposome is that it reduces the immunogenicity of the immunoliposome (antibody coupled immunoliposome) upon repeated administration (see page 6, col. 2, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to make antibody fragment such as Fab' as taught by Harlow et al using the whole anti-HLA-DR antibody as taught by Catin et al and then coupling the antibody fragment to the liposome which comprises a mixture of diacylphosphatidylcholine and diacylphosphatidylglycerol in a molar ratio ranging between 10:1 and 1:1, wherein the acyl chains are either saturated or unsaturated and have between 14 and 18 carbon atoms in length as taught by the '027 patent. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to use antibody fragment instead of a whole antibody when coupled to liposome is that it reduces the immunogenicity of the immunoliposome (antibody coupled immunoliposome) upon repeated administration as taught by Desormeaux et al (see page 6, col. 2, in particular). Harlow *et al* teach that fragments of antibodies can overcome the problem of capping and internalization of the antigen on mammalian cell when using multivalent antibodies (See page 626 in particular). The '027 patent teaches coupling of antibody molecule to the liposome enhances the targeting of the drug encapsulated liposome to the specific cells that are HIV reservoirs as well as marked improvement of the pharmacokinetics of drugs (See col. 4, lines 11-13, abstract, in particular). Catin et al teach HLA-DR protein is one of the most abundant host derived protein acquired by HIV-1 and HIV-2 and HLA-DR protein is expressed on the surface of lymphoid cells such as

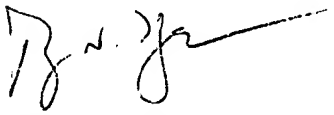
CD4+ T lymphocytes, and monocyte derived macrophages which is an obvious target for such strategy (see page 1922, col. 2, in particular).

13. Claim 9 is free of art.

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Thursday from 9:00 a.m. to 6:30 p.m. and alternate Friday from 9: 00 a.m. to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (571) 273-8300.

16. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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February 2, 2007